UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF PENNSYLVANIA

IN RE:	)	2:12-md-02342-CMR
	)	
ZOLOFT (SERTRALINE	)	September 2, 2015
HYDROCHLORIDE) PRODUCTS	)	A.M. SESSION
LIABILITY LITIGATION	)	10:05 a.m.-12:49 p.m.
J. RETTENMAIER USA LP	)	Philadelphia, PA

DAUBERT HEARING
BEFORE THE HONORABLE CYNTHIA M. RUFE

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I N D E X

P R O C E E D I N G S

THE CLERK: All rise.

(Call to Court)

THE COURT: Good morning, everyone.

ALL: Good morning, Your Honor.

THE COURT: Please be seated. Did we give everyone a chance to set up the electronics and everything else?

MS. YATES: I believe so, Your Honor.

THE COURT: All right. Dr. Jewell.

MR. ZONIES: Your Honor, may I approach with --

THE COURT: Oh, yes, thank you, Mr. Zonies. Dr. Jewell, please resume the stand. Thank you. Good morning.

THE WITNESS: Good morning.

THE COURT: All right. You remain under oath, Dr. Jewell. Please be seated. Ms. Yates, cross-examination, please.

MS. YATES: Thank you, Your Honor.

CROSS-EXAMINATION

BY MS. YATES:

Q. Good morning, Dr. Jewell. Nice to meet you.

A. Good morning.

Q. Doctor, I wanted to start by talking a

little bit about overlapping populations. And I'd like to start our conversation to see if you agree that if one study is a subset of another study, there's really only one study to consider, correct?

A. Well, it depends on the context of the question. If, as we were discussing yesterday, one study is subsumed in another because a second study follows a new set of women for a new set of years, then there's no -- the information in the first study is entirely contained in the second. But on the other hand, as I discussed yesterday, there's still interest in seeing if the information from an earlier period of time is confirmed by independent information in the same population at a different point or different interval in time.

Q. Let me be a little more specific, Doctor. I'm specifically referring to the two Swedish studies, Callen and Reis Callen (ph), 2010 -- 2007 and 2010, Doctor, and you have previously testified that Callen 2007 is a subset of Reis Callen 2010 and there's really only one study to consider, correct?

A. Yes, in that case, in the Swedish case, one is completely subsumed in the other.

Q. Okay.

A. As I just described here.

MS. YATES: And, Your Honor, may I move around again.

THE COURT: Yes.

MS. YATES: Thank you.

BY MS. YATES:

Q. And I think, Doctor, sorry, this is what we're referring to, right, that Callen is a complete subset of Reis-Callen, and those are the two studies we're specifically referring to, correct?

A. I pronounce it Collin, but --

Q. And I think Collin pronounces it even more complicated, okay.

Okay. Let's move from Sweden, Doctor, to Denmark and I think we have your graphics up, by the way if I -- is it better if I pull this a little further forward?

A. Sure.

Q. I think this is your graphic on the three Danish studies, Doctor, Cornum, Pedersen and Jimenez-Solem; is that correct?

A. That is correct.

Q. All right. And you testified a little bit yesterday about these studies, and you do agree, sir, that certainly there are some overlap in these populations, correct?

A. Absolutely.

Q. Now, yesterday you said that Cornum was the first step, and that -- and that's four counties, right?

A. Well, I actually misspoke I think yesterday. I think Pedersen's paper predates the Cornum paper.

Q. Correct, you did misspeak yesterday.

A. The order is Pedersen followed by Cornum, followed by Jimenez-Solem.

Q. Right. So when yesterday you said Cornum was the first step, but Pedersen tried to replicate.

A. The other way around.

Q. You were wrong.

A. It was the other way around, yes.

Q. Well, so Pedersen was the entire country and then Cornum was just four counties.

A. That is correct.

Q. Okay. Now, let's take a little look. Cornum covers 1991 through 2007, correct?

A. That looks roughly right from the graphic, yes.

Q. Yeah, it's a little late on dates, isn't it, Doctor, it's a little closer to 1990. If we divide that area in five, it's probably closer to here, right, if we divide it in five? '91, '92, '93, '94,

fair? So we go a little too long on your chart, right?

A. I can't remember, if I went back to the original paper if it was 1991 or 1990. That looks like 1990 there from the graphics.

Q. Well, should we -- would you like to check Cornum, do you have your binder of studies?

A. I do, yeah, I'd be happy to.

Q. Let's check Cornum.

MS. YATES: And, Your Honor, I have another binder of studies that I don't know if it's identical to Dr. Jewell's, so if I may provide the Court one and the witness, just so we're on the same page.

THE COURT: You certainly may.

MS. YATES: Just in case there's one not in the binder. Thank you.

THE WITNESS: Okay.

BY MS. YATES:

Q. Can you confirm that Cornum is actually 1991?

A. Yes, 1991 I think to 2007.

Q. Right.

A. So that green line, I'm happy to move it over a little bit, if you would like.

Q. A little too far over, right? It doesn't cover 1990.

A. It doesn't, apparently not.

Q. Okay. Pedersen is 1996 to 2003.

A. I'd have to check but that's approximately what I remember.

Q. Okay. And Jimenez-Solem 1997 to 2009, correct?

A. I'd have to check, but that sounds reasonable according to my memory.

Q. Doctor, if you want to check.

A. It's up to you. I don't mind checking if you like, but I'd had to take your word for it.

Q. Okay. All right. So you will agree, sir, that for the years 1996 to 2003, Cornum is a subset of Pedersen, right?

A. Correct. And the Cornum covered just a geographic region of Denmark and Pedersen had the whole national registry at that point.

Q. Right. So we've got a subset in that section, right?

A. Correct.

Q. And so there's no new data under the Reis, Callen-Reis analogy, that's overlap, correct?

A. Sorry, I didn't --

Q. For those years?
A. I don't understand your question.
Q. These two studies, Cornum is a subset of Pedersen for these years.
A. For those specific years, yes, but Cornum has these additional years as you've pointed out.
Q. I understand. If we move to Pedersen, Pedersen is a complete subset of Jimenez-Solem, except one year, '96 to '97, correct?
A. That is correct.
Q. Okay. So let's take a look at the Cornum '91 to '96 non-overlapping date, okay, Doctor?
A. Not overlapping with Pedersen or with Jimenez-Solem or?
Q. It doesn't look like it overlaps anything, right?
A. I'm not sure. I'm sorry, I just don't understand. You want to look at one piece of the Cornum data that's not in either Pedersen and Jimenez-Solem; is that correct?
Q. Right.
A. Okay.
Q. This right here, this green part --
A. Okay.
Q. -- that we --

A. Okay.

Q. Sure. Okay. Now, Cornum looked at four counties in Denmark, correct?

A. Yes, that's my memory.

Q. Sir, did they look at all four counties for all years of their study?

A. I'd have to go back and look at the paper to have that level of detail. I remember it was not the entire country.

Q. All right. Well, let's go to Cornum page 30, sir, and see what counties they studied for the years '91 to '96.

A. Yes, they studied some different counties depending on the year. They covered North Jutland County from 1991 to 2007. They covered Aarhus from 1996 to 2007, and then they covered Ringkjobing and Viborg Counties from 1998 to 2007. So there's overlap in the years there, but not all those counties were covered for the entire 1991 to 2007 period.

Q. All right. Let me take you back, Doctor, to the little area we were talking about, '91 to '96, sir. The only county they studied in that time frame is North Jutland, correct?

A. If -- yes, in that -- if, in that particular left-hand part of the green there, that is -- sorry, I

lost your train of thought there. Are you saying North Jutland County was the only county in 1991 to 1996?

Q. Yes.

A. Yes. Then I agree.

Q. Okay. And they added the other counties that finally made up the four after 1996, correct?

A. That is correct. And the non-overlap with Pedersen to the right involved more counties than the overlap --

Q. Okay.

A. -- non-overlap to the left.

Q. So this number on the left, by the way, represents the total number of women in the entire study, right?

A. That is correct.

Q. And we know that number is not right for this one county for five years, correct?

A. No, of course not.

Q. Okay. This is the whole bar, so --

A. Correct.

Q. -- you know, it's one county, it's a small percentage of that, right?

A. Correct.

Q. Okay. And we know that in the entire Cornum

study, there were 352 patients who took Zoloft, correct?

A. In the entire study?

Q. Yes.

A. Again, I don't have those numbers in my memory, but I can take your word for it.

Q. Well, we can go to -- or we can go to page 33, table 2, Doctor.

A. Fine.

Q. 352 patients using Zoloft --

A. Sorry, could you go a little slower when you're checking?

Q. Absolutely.

A. Thank you. Or put it up on the screen, that's even better.

Q. Sure.

A. Except --

Q. Table --

A. -- it needs to be focused.

Q. -- 2, page 33.

A. Can you focus it?

THE COURT: It's too small.

MS. YATES: Yeah, he's searching for the pull out I think.

THE WITNESS: There we go.

THE COURT: Is that better?

THE WITNESS: That's better, much better, thank you.

BY MS. YATES:

Q. Okay. Right, Doctor, the study, length of study 352 sertraline which is Zoloft users, right?

A. Correct.

Q. And that's four counties over 17 years that got that total.

A. Correct.

Q. Sir, do you know the birth rate in North Jutland for the years 1991 to 1996?

A. I certainly don't know that from my memory, no.

Q. Do you know the population of North Jutland 1991 to 1996?

A. Not precisely, no, not off the top of my head.

Q. All right. I assume it would be important for you to know when Zoloft was approved for use in Denmark, sir. That way you can figure out if women in Cornum actually got Zoloft, right?

A. Well, I -- the table you just put up described the number of individuals in the Cornum study who took Zoloft.

Q. Slightly different question, Doctor.
A. Uh-huh.
Q. I assume it would be important for you to know what year Zoloft was approved for use in Denmark, so that you can actually figure out the timeframe that women could have been exposed to it, true?
A. No. I was just referring back to the original author's Cornum and their description over those time periods over the number of pregnancies, for which they had out -- birth defect outcomes and their subcategories of how many of those women were exposed to Zoloft.
Q. Right, Doctor, but I'm talking about non-overlapping data right now, so let's stay focused. '9 to '96, we already know it's one county not four, right?
A. Yes. But if you're going to talk about non-overlapping data, you have to put in the right-hand side where you're comparing Cornum and Pedersen.
Q. Sir, I promise you I'm going to cover this entire chart, stick with me.
A. Okay.
Q. I have to break it down into sections, okay.
A. Okay. I'm just going to point out that when it takes us off track.

Q. '91 to '96 were one county.

A. Correct.

Q. Right. Now, wouldn't it be important for you to know what year Zoloft was approved in Denmark to find out when women could've been first exposed to Zoloft?

A. Not with regard to the overlap, no.

Q. Okay. Let's take out the overlap then. Wouldn't you like to know when Zoloft was approved, so that you can determine whether the women exposed in a certain timeframe could've taken Zoloft?

A. I took the data as reported by the authors of the study that when they said a woman took Zoloft, I had to take that at face value. I could not undercut their reporting of the data.

Q. All right. Let's try a different approach. You're familiar with a document called the PSUR?

A. Periodic Safety Update Report, yes.

Q. Right. You refer to it in the appendix of your report?

A. Yes, I probably do.

Q. Okay. Well, let's go to page 523 of that document that you refer to in the appendix of your report, and let's just look when Zoloft was approved -- sorry, and when Zoloft was approved in Denmark.

Approval 2nd of July 1993, correct?

A. You need to focus it just a little better for my eyes.

Q. Not even the pull-out?

A. Not even the pull-out, it's blurry. Maybe it's just me.

Q. I think you said you wanted it to be blurry yesterday. Was that your --

A. When I'm reading words, I actually don't like them blurry. Okay. So that's the date of approval you're telling me there, so --

Q. Right.

A. -- date of approval of Zoloft in --

Q. Denmark.

A. Okay.

Q. Okay. So if that's the date of approval, Doctor, women before that date could not have been exposed to Zoloft, correct?

A. I assume that is correct, yes.

Q. All right. Now, you're familiar with after approval, there's also usually a launch date when the medicine goes on the market, correct?

A. Correct.

Q. Okay. Do you know the launch date in Denmark for Zoloft?

A. No.

Q. Okay. Let's look. Launch date in Denmark January 17, 1994. Do you see that?

A. I do.

Q. Okay. So in the Cornum population, the non-overlapping one county, we know that prior to January 1994, none of those women could have been exposed to Zoloft, right?

A. That is the assumption, yes.

Q. Okay. So no -- okay. And then we do know that for one county, for that one year, some of the 352 from the entire study could have received Zoloft, right?

A. That is the assumption, yes.

Q. Okay. Let's move to the Pedersen data, and this '96 to '97, there's no overlap, right?

A. I'm sorry, I'm lost with you now. You said there's no overlap between '96 and '97?

Q. In the Pedersen data --

A. Oh, with Jimenez-Solem, we've switched now, is that --

Q. '96 to '97, no overlap with Jimenez-Solem, right?

A. Okay. So you just have to be precise, because we were talking about Cornum and Pedersen up

to now, and now we've flipped to Pedersen to Jimenez-Solem.

Q. All right. Stick with me, Doctor.

A. Okay.

Q. The reason I'm referring here to Pedersen and Jimenez is they use the entire country's registry, right?

A. Correct.

Q. So there is some overlap Cornum and Pedersen, but only four counties, let's set that to one side, okay?

A. Okay.

Q. We know that these two, Jimenez-Solem/Pedersen looking at the same registry, no overlap, one year. With me?

A. No overlap on the left for one year, and no overlap on the right for several other years.

Q. Got it. Let's stick on the left for now, Doctor, okay?

A. Uh-huh.

Q. All right. And in Pedersen, for the study years '96 to 2003, so the entire study there were 527 women who filled two or more prescriptions. Do you remember that?

A. I don't remember off the top of my head, the

actual raw numbers from the papers.

Q. Would you like to confirm?

A. It's -- I'm completely within your hands, whatever you would prefer.

Q. Okay. Well, if ever you want to check anything, you just let me know because that's table 3, page 2, okay?

A. Of Pedersen?

Q. Of Pedersen.

A. Okay.

Q. Okay. All right. And then it's a lower number for one prescription, 259, but two or more 527, one prescription 259, right?

A. Okay.

Q. Okay. And that total number of exposed women is for eight years, correct?

A. I believe so, yes.

Q. All right. Now, from '97 all the way up to 2009, certainly those years with Pedersen and those years with Cornum are subsets of Jimenez-Solem, correct?

A. That is the understanding, yes.

Q. Now, another study came out, also looking at Denmark, it looked at beyond Denmark, Finland, Iceland and Norway and Sweden, right, and that's Furu.

A. That is correct.
Q. And that came out in 2015?
A. Yes.
Q. Studied about 2.3 million women.
A. Correct.
Q. And the years that Furu studied are 1996 to 2010, correct?
A. That is my memory, but again I'm relying on memory now.
Q. Okay. So Furu starts '96 and if we go up to -- if we use your scale for Furu, the total number of women in that study goes way off your chart, right, 2.3 million?
A. It's much -- well, it's -- yeah, it's about 50 percent higher.
Q. Fifty percent, this is a hundred and -- well, 1.4 million, right?
A. And 2.3 is a little more than 50 percent higher, yeah.
Q. We've got to get a little bit up there, right?
A. Yeah.
Q. 2.3. And we know it goes to what, 2010. I did not go to art school. So that's Furu, right?
A. Except it's not just Denmark as you pointed

out, it's --

Q. It's bigger.

A. It's not only bigger as you've indicated, it's different countries.

Q. Okay. And they look to the Danish registry as well as others, so Jimenez-Solem and Pedersen are complete subsets of Furu on the Danish data, correct?

A. Correct.

Q. Okay. And then Cornum, what do we have, also a complete subset with the exception of this --

A. Correct.

Q. -- two years that people could have got Zoloft in --

A. Correct.

Q. -- one county.

Now, in your report, Doctor, you say -- strike that.

Let's stick with Furu for a minute. Furu, this big 2.3 million women, found no statistically significant association between Zoloft for several cardiac findings, correct?

A. That is my memory. Again, I can't read off the numbers from the top of my head.

Q. All right. Well, let's go through them. I think it's page 7. Or page 5, Figure 2, sorry. Okay.

MS. YATES: Yeah, you're definitely going to have to enlarge that.

Q. So Furu found no statistically significant association between Zoloft and any cardiac defect, correct?

A. Again, it's too blurry for me to read.

Q. Yeah, we --

A. Can you point me to the --

Q. We're going to pull it out, Doctor.

A. Okay.

Q. Also, you have a hard copy in front of you if that's --

A. That's what I was trying to go to, but it's a little hard to listen and look things up at the same time. Where is it in the binder you just gave me?

Q. It should be in alphabetical order under F for Furu.

THE COURT: And you said page 5?

MS. YATES: Page 5, Your Honor, table -- at Figure 2.

THE WITNESS: Okay. Now, I've got the hard copy in front of me. It's much easier for me to --

BY MS. YATES:

Q. All right. No statistically significant

finding for any cardiac defect, correct?

A. You're talking about for sertraline?

Q. Yes.

A. Yes. It's -- yes, the odds ratio, just to make sure we're looking at the same thing, I'm reading an odds ratio of 1.28. You want the adjusted odds ratio, I assume.

Q. Oh, I think we want the adjusted, don't we, Doctor?

A. Yeah, well, I just want -- I just need to know exactly where you're talking about, because there are a lot of numbers on this table.

So you're talking about the 1.13, 13 percent increase in risk associated with Zoloft with a confidence symbol going from .93 to 1.38. Are we talking about the same number?

Q. Yes. That would be not statistically significant, Doctor, right?

A. At the 5 percent level, that is correct.

Q. Okay. An atrial -- Furu found non-statistically significant finding, atrial and ventricular septal defects, correct?

A. For atrial and ventricular septal for sertraline, yeah, the odds ratio was a 5 percent increase in risk, but with a confidence integral going

from .82 to 1.35, yeah, that's on the screen.

Q. 1.05, right?

A. 1.35.

Q. 1. -- no, I meant the odds ratio.

A. Oh, the odds ratio is 1.05, yes, correct.

Q. Okay. Dr. Furu found no statistically significant association between conotruncal and major arch anomalies, correct? Odds ratio 1.02, confidence intervals .48 to 2.15.

A. Correct.

Q. Furu found no statistically significant finding for an atrial ventricular septal defects, correct?

A. Yes, there we have a much bigger odds ratio, but much wider confidential interval, correct. That's what's correct is what's on the screen.

Q. And same question, non-statistically significant finding for right ventricular outflow tract obstructions, correct?

A. Yes. Again, 40 percent increase in risk, but the confidence interval as described there.

Q. And Furu found a non-statistically significant finding for left ventricular outflow tract obstructions, correct? Oh, did I just do that one, I apologize. Did I do right and left?

A. No, you did right and left.

Q. Okay. Sorry.

A. That's okay.

Q. So, Doctor, while we're talking --

MS. YATES: You can take that down.

Q. While we're talking results and conclusions, let's turn to Jimenez-Solem for a minute. Jimenez-Solem concluded that the significant odds ratio that they reported were not the results of ingestion of Zoloft, correct?

A. Yes. They believed it was due to a sort of unknown confinder associated with filling prescriptions, which I think is a little -- we could talk about that in detail, we didn't --

Q. You disagree with that peer review published opinion.

A. I disagree with that interpretation of the results, yes, as I described yesterday. I think they made the comparison both indirectly instead of directly comparing the pause to the non-pause, which I think gets more directly at the confounding by indication phenomenon.

Q. You disagree with the authors?

A. I disagree with the authors on that interpretation, yes.

Q. Right. Doctor, let's move to Louik. A lot was talked about Louik, corrections. Mr. Zonies, I thought I interpreted as saying, let's just take it out. I say let's leave it in, what do you think?

A. I don't understand what you mean by either what he meant by take it out or leave it in.

Q. I think he said there's so many mistakes in it, just to push it to one side.

A. No, I don't -- I didn't get that from what he said. I certainly don't believe it should be entirely ignored just because of that transcription error.

Q. Okay. So then let's look. You did a -- well, we saw a few forest plots yesterday, now the Court has the benefit of -- and you were kind enough to provide us one, but a large sheet with all those old cardiac findings. That was the forest plot that you went to yesterday; is that right?

A. Yeah, I would call it a visualization rather than a forest plot, but I don't mind if you -- I understand.

Q. Visualization.

A. Yeah.

Q. Now, I may have misheard yesterday. I thought you said that you were not using it for

consistency, but isn't that only what you're using it for?

A. I -- if I said that, that's not what I intended. I wanted it to -- I think what I said yesterday was I wanted a way to put all of the results on a single sheet of paper for ease of reference, and to see the overall span of findings, whether it's for every finding or just the -- all cardiac findings or some of the subcategory findings.

Q. All right. And so I'm clear, you're not using it to support your causation opinion.

A. I'm not using the plot itself, no, I'm using all that data that's on the plot obviously that's going into the opinion.

Q. All right. Now, when you did your first expert report, you had a different forest plot; is that right?

A. I think I had an expert report for a state case, the very first one I wrote that I had a different visualization, that is correct.

Q. Right.

A. I just didn't have it on the log scale, and then I -- we discussed that at deposition, and I agreed that it was better to change it to the log scale.

Q. So let's look at that first forest plot. It was from the Robinson case, which was the case that was tried in the PCCP.

A. I don't remember which case it was actually, I just know it was a state case.

Q. You testified in that case, right?

A. I did, but I've been deposed I think two or three times. I lose track of the cases, it makes no difference to me.

Q. No, but I mean, you were sitting in a witness chair in front of a jury in that case. Do you remember that?

A. You know, I can't even remember the name of the plaintiff, individual plaintiff.

Q. Okay, fine. All right. So this is your first forest plot that was in your state court case report. Does that look familiar?

A. Yes. I still can't see it because it's blurry. It's more blurry than it was yesterday, I don't know why, but I take your word for it. It looks familiar.

Q. It looks familiar. And as you said, that was on a linear scale, right?

A. That was on a linear scale, the visualization, yes.

Q. And, Doctor, it was pointed out to you that a linear scale can distort things even further to the right, right?

A. Well, the point was made when we discussed this at deposition that the area of protection, that's the area on the X axis from 0 to 1 is compressed, because of the asymmetry. And so I agreed with that and was perfectly happy, in fact, a Pfizer lawyer produced the equivalent to this on the log scale, and I was perfectly happy to discuss that one. And now I have got around that, put all of these on the log scale.

Q. Right. Because the linear scale distorts it, doesn't it?

A. Well, it makes it harder for the eye, because if you're going to try and use this in the way I was describing yesterday, with the eye, it's asymmetric between 0 and 1 and 1 to 10, and in this case 1 to 7.

Q. All right. And then actually, you removed the forest plot altogether from your MDL report, right?

A. I think I probably took it out, yes, but I used it as an exhibit I believe in the trial on the log scale.

Q. Right, okay. Now, let me talk about Louik and the correction. Doctor, the correction in Louik had a statistically significant finding of 1.2 corrected to a non-statistically finding, non-statistically significant finding of 1.0, correct?

A. No, that's not correct.

Q. That's not correct?

A. No.

Q. Confidence interval.

A. I know the words, do you want to restate your question?

Q. Sure. It's going to be a long day, Doctor, because I am not a mathematician.

The confidence, the change and correction that was made in Louik, I apologize, the lower confidence interval went from a 1.2 to a 1.0.

A. Yes, the odds ratio stayed the same, and it was the lower bound of the confidence, and the upper bound stayed the same, but the lower bound was changed from 1.2 to 1.0.

Q. Right. And the New England Journal of Medicine when they were corresponding with the authors wanted them to remove all reference to significance, because that finding was no longer statistically significant.

A. There certainly was discussion about changing the emphasis on that. I don't want to say that was their exact words, but I don't think they wanted to remove all mention of it, but I think they felt bound by the fact that it now -- the confidence interval contained one to change the emphasis away from stating it as a statistically significant result, that is correct.

Q. It's more than changing an emphasis, sir. It's removing a word that says statistically significant, because it's no longer statistically significant. That's the standard the Journal uses, correct?

A. Well, we certainly could look at the e-mails and look at their exact language back to Dr. Louik, I don't remember it word-for-word. But they were caught by the fact that their description of how you should emphasize results in papers is influenced by whether the result is statistically significant formulated -- formula. And that's what -- they didn't want just to publish the change in the number. They also wanted to change a little bit of the emphasis of how it was spoken about in the paper.

Q. Right.

A. And we should probably, if we're really

going to discuss that into detail, we should probably put the e-mail up from the New England Journal, because that gives explicitly what they were and explicitly the reaction of the authors to that, which they thought that was crazy, but they still -- the editor thought it was crazy, but they still had to do it.

Q. Right. Because that is --

A. You shouldn't take my word for it, just put the e-mails up.

Q. Actually, sir, why don't we go straight to the correction published by the New England Journal of Medicine. I will -- there was debate in the e-mails about .98 or 1.02 and rounding to 1, right? And that revealed that actually the 1 has been rounded up from .98, correct?

A. Yes. Well, that would be standard in that case.

Q. Right, that's standard. As is the New England Journal of Medicine saying remove the word significance when it's no longer statistically significant, correct?

A. I think that is the standard of the New England Journal, yes.

Q. And that's what the correction -- set aside

the e-mails, we saw them, the correction removes the word significance because it was no longer statistically significant, correct?

A. In the judgment of the Journal that is correct, yes.

Q. Not in the judgment of the Journal, sir, using the standard they use.

A. If you read the e-mails from every statistician involved in that debate, including the authors of the papers, they believe that distinction to be meaningless. The Journal has a formal standard and I -- that's what they use, for better, for worse, that's what they use.

Everyone else in that debate agreed that it was a meaningless distinction. I don't have any debate. The results is not statistically significant. My opinion does not hang on it being statistically significant.

The confidence interval goes from 1.0 to 3. something, 3.8 or whatever it was, the upper band. The entire set of values of the odds ratio that are compatible with the data, in an interpretation of the confidence also has the risk is raised.

Statisticians do not hinge opinions, therefore, in a case where there are multiple pieces

of data on that single statistical significance. I thought we discussed that effectively yesterday.

Q. Do you remember my question?

A. Well, you can certainly ask it again, that's fine.

Q. I'm just asking if you remember it, Doctor.

A. You asked me about whether the Journal said it was statistically significant or not, and I said, no, they said it wasn't statistically significant anymore.

Q. And I think you also said that it really doesn't make much difference, if any, to your opinion because you don't rely on statistical significance.

A. No, that's not what I said. Let me say what I did say, which is in a single study, the issue of statistical significance plays a much greater role because it's the only information we have at that point. And the role of chance has to be addressed.

When you're looking at the Louik paper now in the big picture in that entire list of studies, that's not the sole source of statistical significance, nor the sole source of information about that particular subcategory. And it's important to remember here, we've moved to talking not about all cardiac, but to a subcategory where results are more

variable.

So in that bigger context, the change of a confidence interval lower bound from 1.2 to 1 is important to correct. It did change my viewing of the data, it had to because it changed, but it did not in the end affect my overall opinions.

Q. Okay. I think you said yesterday it had a very slight impact on your opinion.

A. Yes, because as I pointed out yesterday if you look at all of the data on one piece of paper, and then you change -- before the change and after the change, it's almost undetectable to the human eye the impact that change makes.

Q. And the subcategory that changed was all septal, right?

A. That is correct.

Q. And as you've told us several times, your focus was all cardiac.

A. That is correct.

Q. Now, I just want to address something else. There was another correction that the authors are either submitting or proposing to submit, but that has nothing to do with the results, the risk estimates or the confidence intervals, correct?

A. No, that is incorrect.

Q. Okay. Let's put up the e-mail then to Mr. Zonies of August 31.

MS. YATES: Do we have that?

(Pause)

MS. YATES: No, that's not it, so I can find it in the slides? Sorry.

(Pause)

MS. YATES: It's the one that says New England Journal of Medicine correction again. Okay.

Q. This is the e-mail. Doctor, can you read that? Is that clear enough for you?

A. Yes, I can read that one fine, thank you.

Q. All right. So this is the -- this is from Mr. Zonies' slide, this is the most recent correction. And the authors in this e-mail state clearly, "We wish to state clearly, the risk estimates in confidence intervals in the LGA which we provided on July 27, 2015 in response to subpoena are correct." Did I read that correctly?

A. You read that correctly, yes.

Q. All right. So -- and what they're correcting is something about some of the descriptions that talked about the variables, correct?

A. They're describing which variables were used in the adjustments for confounding that produced the

confidence in all they reported in the New England Journal.

Q. Right. So that's a descriptive error, but they're standing by their results, even though all those variables were not specified in the article, correct?

A. They're standing by the results they provided for -- from a re-analysis of the data in July, which we readjusted the data for a slightly different set of confounders than from the set they described in the original journal article. That was the error I detected when I saw the logistic regression.

This is slightly different. Now, it's not a big deal to me. We pointed out because we wanted to get the right results with all this fuss about the confidence interval.

Had they adjusted for exactly the variables they said they did in the article, the confidence interval would change. That's why I'm saying, okay, now they've said, ah, well, actually what we did in July of this year was what we are saying we actually did five years ago, and now we want to go back and change the article from five years ago, and said actually we didn't quite adjust for those variables

the way we described them five years ago. We want to change that. That's what that e-mail describes.

It doesn't matter to me. What it does point out is that if one changed back to the variables that they said they adjusted for, that confidence bound, lower bound could easily be above 1 now. So it's a moving target, it's not a very important moving target for the reasons we've discussed at length.

But this whole fixation about 1 is illustrated again by the fact that if you, in fact, use slightly different sets of variables that lower confidence bound is going to change, not much, but it could go from 1.0 to .99.

Q. Doctor, that is rank speculation on your part.

A. No, it's not speculation. It could easily go from 1 to 1.01, I agree, we don't know, and if you take out -- in and out variables, those lower bounds will change. That is not speculation, that is absolute hard statistical fact, it will not stay the same --

Q. Well --

A. -- if you change the variables.

Q. Let's see if we can breakdown this e-mail because what they're saying is in the process of

reviewing the original regression analysis, which we retrieved in response to the subpoena dated July 15th, 2015, and which was provided on July 27th, we discovered some inconsistencies between what was included in that analysis and what appeared in the New England Journal of Medicine report, right?

A. That's what they said. Yes, actually I discovered the inconsistency and pointed it out, but this is what they are sending back to the Journal now.

Q. I got it. They're saying, here's our data based on variables, here's our results based on those variables, but the variables that are actually stated in the New England Journal of Medicine there's a few missing.

A. Yes, that is correct, and the way they described one other set of variables was not correct in the paper, that's described later on about the variable where they described the history of a birth defect in a first degree relative that was wrong, taking their word for it. That should've read history of a cardiac defect in a first degree relative, so that's a little different. I assume they mean cardiac birth defect.

And the way they described the adjustment for the year of lost menstrual period was sloppy in

the New England Journal, and they regretted that they didn't get that more accurately described, you know, but basically, they didn't get the description of the variables in the article to correspond to the description of the variables in the analysis they provided to the Court.

Q. Right. But the -- so they're going to now make sure the description does match. We don't even know if the New England Journal of Medicine is going to correct it, do we?

A. I have no idea, no. This is fairly recent, so I don't know. And by the way, this is completely insufficient, because in principle, does that mean that all the numbers in that table, forget sertraline and septal, all the other SSRIs, do they also need to have those adjustment variables changed. Were all the analysis done with this new set of variables that they produced in July or not, I don't know.

Q. Doctor --

A. Only they know.

Q. -- I'm not sure if we're just not connecting or you're misinterpreting, but they get -- they do the data analysis based on a set of variables, right? And they have those results, and they stand by those results.

A. This is the analysis done in July, yes.
Q. Correct?
A. Correct.
Q. Now, they go to their paper and it doesn't -- some of the variables are missing in the description.
A. Correct and misstated also.
Q. And so they stand by their risk estimates and confidence intervals.
A. They -- what they say --
Q. They say that.
A. What they say here is in the confidence intervals provided in July are the variables they wish to now adjust for, and they don't correspond with the variables, they said they adjusted for back then. I think what -- to the best spin on it, they're saying that's what we meant to say five years ago in the paper. These were the variables we intended to adjust for, we got it wrong in our description of the table, we made a transcription error. We also got the description of the confounding variables incorrect, and now we have to change that. That's the most positive spin I can put on it.
And I assume that in fact, that change in the list of confounding variables applies to every

number in that table, because there are a lot more numbers in that table than simply the Zoloft or the septal heart defect number.

Q. If they did their analysis on variables A through J, but H, A, B, and D are not reported, and now they're just going to clean up the reporting and make sure they're all in there. That does not affect the results they found, sir. It is correcting the description of what they looked at.

A. That is the most positive spin, but it makes the point that had they produced an analysis in July, that corresponded to what they claimed they were adjusting for in -- five years ago in the New England Journal, that lower confidence bound will change a little, not importantly.

But that's why in a sense, this is all a tempest in a tea cup. Because if you put in or leave out one of these variables, that confidence interval bound may well slip below 1. The confidence interval for the original reporting of this data differed from what they produced in the New England Journal.

Confidence interval bounds change a little bit, not just because the data is changing, but as you put in a confounding variable or not, even if that confounding variable is irrelevant, it will change

them a little bit. And that's why statisticians don't put a tremendous amount of emphasis on the upper and lower bounds of a confidence interval. It's misplaced emphasis.

And, in fact, to be frank, this whole discussion is a misplaced emphasis on not where the truth is, but on the periphery. It's not important, but it does make a point that which variables you put in, will change the confidence interval, and it may make it a little bigger, it may make it a little smaller. That's why the exact value isn't that crucial.

And none of these, by the way, are changing the actual estimate of the increased risk, which has remained at 2 pretty much throughout their reporting of their data.

Q. Do you remember my question?

A. I think I answered the question.

Q. No, do you remember my question, sir?

A. Well, we can go back and you can read it to me again.

Q. No, I'm trying -- we have an amount of time, and I'm --

A. I'm happy to stay here as long as you want.

Q. Well --

A. And if it helps you to reread the question, it sure helps me, so please do.

Q. If the examination -- the analysis was done on a data set A through K and they have the results, and we have those results, but what is actually in the article is missing B, C and D, and now they're going to correct the description.

Correcting the description does not change the results of their analysis, yes or no?

A. No, it doesn't change the results. The results correspond to a specific set of confounding variables. What does change is if you change the choice of the confounding variables. And the choice of the confounding variables is different in the paper than in the analysis they ran for the Court. That's the only point this e-mail is dealing with.

Q. I must -- I'm going to move on, I must not be communicating.

Let's go to your forest plot that was used I believe in the Robinson trial and the one that you used obviously has been in here has been updated, right? There are more studies, right?

A. There is some new studies, yes.

MS. YATES: And I may need to pull this a little closer, Your Honor, I apologize.

THE COURT: yes.

MS. YATES: May I just --

THE COURT: You may hold it there, if you can pick up everyone's voice.

BY MS. YATES:

Q. So on this one, appropriately so, we have Louik at that time, because it was showing a statistically significant result, right?

A. Correct. It was -- the 1.2 is what's changed.

Q. Right. And now it's gone down into the black zone.

A. I moved it down because it's not significant anymore --

Q. Right.

A. -- according to the New England Journal. And I've of course moved the 1.2 to 1 so it just clips the line at 1, as we saw yesterday.

Q. Okay. Now, this is a log scale, right?

A. Correct.

Q. And when you do a log scale, the odds ratio is right in the middle of the confidence intervals, correct?

A. Correct.

Q. And if we look at Louik, it's not, is it?

A. That's very slightly off center, and that's I think what Dr. Kimmel noted and that's what led to that discovery.

Q. Right. But you didn't notice that out of all of these studies, there was something wrong with the Louik data, based on your own forest plot.

A. No, I confess, my eyes are not that good, I did not see that asymmetry, no, in that one particular confidence interval. It's not very asymmetric, but it is a little bit.

Q. It sort of jumps out, doesn't it, Doctor?

A. Well, I guess it didn't to me. It may have to you. And it's corrected now, so I --

Q. Okay. The good news when I turn pages means that we've covered it. All right. At the time of this earlier forest plot, sir, Louik was the only statistically significant finding on septal defects that was -- that replicated something from the Denmark studies, correct?

A. Yes. If you lump all three, there were the Danish studies which have some form of replication as I discussed yesterday and we discussed earlier, but if you put those altogether, then the only other study of the ten or so that were in there at that point was the Louik one with regard to all septal.

Q. Okay. Well, we didn't talk about replication, Doctor, we talked about overlap, right, two different concepts.

A. Well, the whole point of the overlap is the idea of replication and whether we're getting any new information from separate studies of this overlapping populations.

Q. All right. Doctor, let's change subjects. Let's go to Berard 2015 paper, okay.

A. Sure.

Q. You recall testifying in February 2015 Frye hearing before Judge Bernstein?

A. I do remember the experience, yes.

Q. You were asked about Dr. Berard's study.

A. I was by the Pfizer lawyer, yes.

Q. And you were asked whether you could check Dr. Berard's calculation from her paper, right?

A. Correct.

Q. You were asked if you could calculate the odds ratio.

A. I was.

Q. And you testified you could do that.

A. I did.

Q. And, in fact, during the break in a hearing, you calculated the crude (indiscernible) ratio to be

1.3, correct?

A. Well, I don't remember the actual number. It depends on -- I think there were several in her paper, but I did one that they were asking me to do at the hearing during a break, and I confirmed her calculation.

Q. No, well, let me show you your testimony. You don't remember that it was 1.35?

A. No, I don't remember the numbers.

Q. All right.

MS. YATES: Let's bring up the transcript.

THE COURT: Do I really care what Dr. Berard says and whether he can calculate her numbers?

MS. YATES: Well, if there's a mistake in her paper and it's the only other statistically significant finding, Your Honor, I don't know.

THE COURT: Unless he depends on it.

BY MS. YATES:

Q. Doctor, let me --

MS. YATES: You know what, Your Honor, let me cut to the chase.

Q. We've seen that there are two findings within Dr. Berard's paper that are statistically significant, but that there is certainly debate as to

whether there are mistakes in those two numbers, right?

A. There was a debate in those two numbers, and those are the two that changed the most from the crude calculations that were done based on raw data from the paper that Dr. Kimmel most specifically did the whole set.

As I discussed at some length yesterday, the dispute is about the confidence intervals, and therefore the level of statistical significance. Dr. Berard claims in her paper to have used a more sophisticated statistical methodology for calculating the confidence intervals that she's forced to do because of the multiple pregnancies for women that -- that doesn't occur in almost all these other studies. There's a little bit about that in Furu by the way that we could discuss.

That's -- there's no debate about that as far as I'm aware. I've, as I said, told people that's the reason why there is this discrepancy between these crude calculations that everyone is doing, and what Dr. Berard and her team have reported. And she was explicit about checking the numbers, pointing this out that, in fact, she had to deal with this issue with multiple pregnancies. And I don't believe there's any

debate about that, as yet, that --

Q. All right. Are you aware --

MS. YATES: And, sorry, Your Honor, I do have to go into it apparently.

Q. Let me show you a slide that I believe was used in opening by Mr. Cheffo and this is Dr. Berard's 2015 paper, I'm trying to -- so let's just look at the title. All of the Zoloft findings match and are confirmed as non-significant, okay.

So when you go to OpenEpi, every other result in Dr. Berard's 2015 publication, you plug in her numbers on an OpenEpi and they're correct.

A. Well, they're not correct. They coincide with Dr. Berard's calculations using the more complicated software.

Q. They coincide.

A. Correct.

Q. Okay. And then we come to the two statistically significant findings in her paper and they don't coincide on OpenEpi, right?

A. No, the OpenEpi here, if her description of her data is correct, would be an incorrect statistical procedure to use for this data because it doesn't deal with the issue of variability correctly when there are multiple pregnancies per women.

Q. Doctor, are you aware that Dr. Berard did an abstract in 2013?

A. I think I am aware, and I think in there, she had crude results that she subsequently updated in her paper.

Q. And that abstract is the paper that later was published, right?

A. Well, it's a precursor. I mean, the -- usually papers change a little bit from an abstract and it did in this case, is my memory.

Q. Okay. And all of her numbers in the abstract except those two findings that become statistically significant match the other paper, right?

A. I'd have to check. But my memory is the use of the generalized estimating equation approach probably happened between her abstract and her paper. That would be my guess.

Q. And that's a guess, right, Doctor, because you don't know?

A. Well, all I know is that Dr. Berard herself said that she had pointed out that people were misinterpreting her papers' results by applying OpenEpi calculations because they were not paying attention to the multiple pregnancy issue, and that

she had indeed used a more sophisticated piece of software and had rerun the analysis on request, and checked the results of the paper.

As I testified yesterday, beyond that I have no way of checking --

Q. Right.

A. -- if Dr. Berard is either telling the truth or if --

Q. If the data is accurate.

A. Well, let alone whether the data is accurate, whether she did the analysis correctly from raw data, I haven't got access to that data.

Q. All right. So you think we have the abstract and then she does this GEE modeling, right, for the paper and that's what changes the two results according to Dr. Berard.

A. Well, you would expect it to change --

Q. No, no, please, Doctor, just answer my question. That's what Dr. Berard says, right? We have the abstract, and then in the paper she uses the DEE model and that changes these two findings and they are no longer -- they no longer coincide with OpenEpi, because she used this modeling, right?

A. That's the speculation of the difference between the abstract and the paper, yes.

Q. Okay. Let's go to tab 203, please. Doctor --

MS. YATES: Show the title, please.

Q. This is Dr. Berard's 2013 abstract, sir. Okay.

A. Okay.

Q. She used the GEE model in her abstract, didn't she, sir?

A. Apparently. So my speculation of why there might be a difference between the abstract, so we are back to the beginning of saying she used the GEE models, I have to take the paper as the -- the peer review paper as the final version. I can't -- you have to ask Dr. Berard why there's a difference in the abstract, I don't know. I've done my best to speculate.

Q. Right. And in fact, Dr. Berard, in her abstract, came up with numbers that matched OpenEpi didn't she, using the GEE model?

A. I haven't checked that, but I believe that's correct, yeah.

Q. Okay.

A. That's what made me speculate that, that it looked like OpenEpi but --

Q. All right. So you asked for Dr. Hubrix's

data, have you asked for Dr. Berard's data to try and confirm what she did?

A. No, I asked her to confirm and she did, but I have not gotten that data myself. I would get it for the same reasons that I haven't been allowed to get Dr. Hubrix data. I'd love to have the data for all of these studies, the raw data, but that would be a two-year project to confirm the results of every single paper in the peer reviewed literature.

Q. Okay. My question was just did you ask for her raw data?

A. And as I indicated and answered, I asked for her to confirm the results, which she claims she did. Actually she claimed her statistician confirmed the results.

Q. All right. Let's move on a little bit, Doctor. Your qualifications are in mathematics, correct?

A. No.

Q. Don't you have a degree -- a Ph.D. in mathematics?

A. I do, but I don't believe that's -- Ph.D. is the sole total of my qualifications. God forbid.

Q. I didn't say that, but, Dr. --

A. Didn't you ask me that my qualifications

were only in mathematics?

Q. I don't think I said only.

A. Oh, well they're not in mathematics solely either --

Q. Okay.

A. -- they're -- I have some qualifications in mathematics, less and less as I age.

Q. You're a self-taught statistician, right?

A. I sometimes describe myself as that. That's a little unfair to people whose lectures I sat in in my post-doctoral training where I got very good mentoring.

Q. So are you --

A. I think that's a little bit egotistical to put it as completely self-taught.

Q. I'm using your words, Doctor.

A. I indicated I often describe myself that way because I didn't take -- do a graduate program in statistics.

Q. Okay. And your opinions that you're offering today of Zoloft can cause or contribute to all cardiovascular birth defects, correct?

A. Correct.

Q. You're not a teratologist?

A. No, I'm not.

Q. You don't know what the teratology community requires before concluding there's causation?

A. I've been given documents like that at deposition, but I certainly couldn't repeat them word for word, and it's not my community, that is correct.

Q. No medical training, not a medical doctor?

A. I'm not a medical doctor, no.

Q. Birth defects is not your area.

A. Well, I have no specific area, but certainly I have not worked in birth defects as my specific area of application, no.

Q. And outside of your work as a litigation expert on behalf of plaintiffs suing Pfizer, you have not opined that Zoloft causes congenital heart defects, correct?

A. No, I'm trying to do that now with a joint paper with Hubrix, but that remains to be seen if I can succeed.

Q. Right. Did she get back to you after her polite too busy?

A She said no, she did get back to me as we described yesterday, said she thought she would try and get some of her team to help, but we haven't connected since then.

Q. Right. You started working on the Zoloft

litigation before Dr. Berard actually submitted her report in the MDL, right? You were already consulting with the plaintiffs?

A. That I can't swear to. I don't -- I was not involved in that first MDL as far as I'm aware --

Q. Right.

A. -- so I don't know the timing of when I was contacted, vis-à-vis, that hearing.

Q. Okay. Can we go to tab 154 -- oh, so we're mixing apples and oranges, Doctor. I didn't say hearing --

A. Oh.

Q. -- you were already an expert for plaintiffs when those reports, including Dr. Berard's, went in in the MDL, correct?

A. That I don't recall, I may well have been, I just don't -- I wasn't paying attention to those dates of her reports as to when I was contacted.

Q. Do I need to check?

A. No, no, I take your word for it.

Q. All right.

A. If you have the dates there, I --

Q. Okay.

A. -- you have them.

Q. All right. You've not published any

articles regarding congenital heart defects?

A. No, that's not my area of -- my personal area of research.

Q. You've not published regarding any other types of birth defects?

A. No, as I indicated, that's not my personal area of research.

Q. You've not published regarding Zoloft or any other SSRI?

A. No, I publish about GEE, not about birth defects.

Q. Right, that model.

A. Correct.

Q. Okay.

A. That model.

Q. Popular paper though.

A. It is a very --

Q. Correct?

A. -- highly cited paper, yes.

Q. That's what I heard.

You don't claim to be an expert in the field of cardiovascular medicine?

A. No, I'm a statistician.

Q. And you don't claim expertise to be able to tell the Court whether or not heart defects are

anatomically, clinically, or developmental heterogeneous, correct?

A. No, that's not my -- you should talk to a cardiologist or an expert if you want to get into the fine details of those conditions.

Q. But what you do agree from your perspective, is that it is important to perform sub-analyses on specific heart defects, correct?

A. As part of my methodology as I described yesterday, you have this conundrum when facing a question of risk when you're dealing with a rare outcome, and we discussed that length yesterday, I'm happy to go over it again, which determines the level of subcategorization that seems reasonable to the experts -- not to the statisticians, but to the experts -- and yet provides enough data for the statisticians to say we can get some level of definitive estimates of risk. And that's how I use it. And then only when you find something of interest in the larger subgroup where you've got some level of statistical precision to say something does it make sense to look at the subcategories and say, yes, I believe we have a signal here with regard to the larger category. Now as a next step in the methodology let's look at the subcategories to

determine whether in fact systematically one subcategory does not mirror that association you already determined. That's the methodology.

Q. Doctor, do you agree that it is important to perform sub-analyses on specific heart defects?

A. Only in the sense -- that only makes sense to me if you've determined a priori that there is a signal in the larger group. Otherwise it doesn't make sense to go down one, because if you find positive findings in the subgroup they're going to be very statistically imprecise. If you don't find anything you're no further forward.

So my feeling is you look at the subgroup where you have some level of statistical precision and then you go and look at the subgroups.

Q. Okay. So you look at the subgroups to the extent the data permits it?

A. Yes, I think --

Q. All right.

A. -- fair description.

Q. Doctor, you agree that replication is a crucial part of assessing causation?

A. Yes.

Q. And you agree that consistency is also an important part of assessing causation?

A. It is a part, yes.

Q. And it's -- you agree that it's also important to assess potential biases, including confounding, especially when the evidence is coming from observational studies, correct?

A. Correct.

Q. And that's what we have with Zoloft, right?

A. Correct.

Q. Couldn't do a randomized control trial could me?

A. No, unfortunately -- well from a statistician it's unfortunate, from a women's perspective maybe it's fortunate. It's not ethically possible.

Q. Doctor, I need to shift gears a little bit to talk about meta-analyses.

You rejected the Miles and McDonagh peer reviewed published meta-analyses in your report on Zoloft, correct?

A. Well, I didn't reject them. I don't find them particularly scientifically reliable or helpful in addressing the overall question. I discuss them in the MDL report.

Q. You discussed and you rejected as forming part of your opinion, correct?

A. That is correct. It did not influence my opinion, and I think that is fair to say

Q. And in Prozac you focused your attention on the available meta-analyses, correct?

A. Yes, as I discussed yesterday in the Prozac case it started for me with the fact that Eli Lilly themselves, the manufacturer, had done their own meta-analyses, which I focused on, not specifically the large one, though it's -- Prozac is discussed in the large meta-analysis. So the manufacturer there had already done as part of their protocols a full meta-analysis of the question of whether Prozac raises the risk of certain kinds of birth defects.

Q. So that was a yes?

A. Yes, and that's not available to me here, because as far as I'm aware Pfizer has not done a meta-analysis, they did not consider that to be part of their methodology of addressing this question. And I can't speak for Pfizer obviously as to why they choose not to use a meta-analysis. But there is no one that I'm aware of.

Q. You do agree, sir, that both Miles and McDonagh are both published peer reviewed meta-analyses that looked at Zoloft and cardiac birth defects, right?

A. Yes, certainly Miles is, and I think that McDonagh was part of a very large report, which was published. I don't remember the peer review status of McDonagh.

Q. All right. Let's -- we'll come to it. Let's take a look at Miles. And let's look at their objective, okay? And that's from the Miles abstract. And we'll put it out.

Miles' objective was to determine the strength of the association between individual SSRIs and major/minor and cardiac malformation among infants born to women taking these medicines, right?

A. You read it correctly.

Q. And they followed a specific method, right, called Moose (ph)?

A. They did.

Q. Okay. And if we go to the -- continue on the abstract. The study found -- the meta-analysis found that for Zoloft and Celexa that they were not significantly associated with congenital malformation, correct?

A. Yeah, I'm sorry, I can't follow on the screen, it's just blurred.

Q. It's Miles' abstract. There it is. It just takes us a minute to pull it out, Doctor.

A. Okay. That's fine. It's just when you're reading I can't -- I just wanted to let you know I can't follow along with you.

Q. Okay. So Sertraline and Citalopram were not significantly associated with congenital malformations, correct?

A. You read that correctly, yes.

Q. All right. And in their section on page 1007 reporting the results of cardiac malformations the report states that Zoloft was not significantly associated with increased odds of cardiac malformations, correct?

A. Sertraline. Sertraline, yes.

Q. Well you know Sertraline is Zoloft, correct?

A. Yes, that's correct.

Q. All right. But it did show that some of the individual agents, Paroxetine was significantly associated, correct?

A. Paroxetine. I've lost Paroxetine in this paragraph. I'm sorry, I'm not following you.

Q. I think it's right above.

THE COURT: Read the first sentence.

THE WITNESS: Oh, there it is. Yes, it's -- I was looking for the ones at the bottom where the drugs are highlighted.

BY MS. YATES:

Q. I apologize, Doctor.

A. That's okay. Yes, Paroxetine was significantly associated in their meta-analysis with cardiac malformation.

Q. And that's Prozac?

A. That's Prozac, correct.

Q. All right. And the others were not, including Sertraline, which is Zoloft?

A. Correct.

Q. Okay. And in fact the authors conclude -- well let's just take a look at figure 2, if we can. The meta-analysis reported an odds ratio of 0.931 for Zoloft and cardiac malformations, correct?

A. This is -- yeah, I'm not sure what you're pulling out here. You've got Pederson on the left there with numbers for CHD. Is that the Pederson results? And then underneath that, is that the meta-analysis?

Q. So, Doctor, these are all the study names, right? You know how meta-analysis goes, right?

A. I -- to be frank I just can't read this, the page.

THE COURT: I think he needs to refer to the hard copy.

THE WITNESS: Yeah, why not--

MS. YATES: All right. I think that's a good idea.

THE WITNESS: Sure. That's --

BY MS. YATES:

Q. Why don't you pull out the hard copy, Doctor.

THE COURT: And it is an appropriate time to take a brief recess in the morning, so we'll do that now, and come back with hard copies for all of us.

THE WITNESS: All right. Thank you.

(Recessed at 11:20 a.m.; reconvened at 11:43 a.m.)

THE COURT: All set?

CROSS-EXAMINATION, CONTD.

BY MS. YATES:

Q. Hello again, Dr. Jewell.

A. Hi.

Q. Now you met with the lawyers during the break, but I assume you didn't talk about your testimony because you know you're under cross-examination, correct?

A. Do I have to say what I talked about?

Q. Well if you talked about your testimony you

weren't supposed to.

A. I asked the way to the bathroom and they -- in the side there.

Q. No problem. You didn't know that from yesterday?

A. This is a big place, I'm not paying attention to the location of the restrooms.

Q. Okay. But you didn't talk about your testimony?

A. No.

Q. Okay. We left off, Doctor, at Miles, figure 2 and the result for Zoloft. So, I think you have that now in hard copy, but we also were able to pull it out. All the studies are listed, right, Doctor, with the results, and they plot the odds ratios and the confidence intervals, rights, and then they have a final result for Zoloft, correct?

A. Correct.

Q. And that odds ratio for Zoloft is .931, correct?

A. Correct.

Q. And that's cardiac malformations?

A. Correct.

Q. And in fact if we turn to page 1011 you said yourself that when the studies are done you've got

your statisticians and then you've got your medical people, right?

A. I don't know in this particular case who's involved.

Q. Okay. Well we could look, right?

A. Well we know the authors names, yes.

Q. Right. And some of those are medical doctors?

A. You know I haven't looked, I don't know. I don't know -- these are from New Zealand I think. I don't know them.

Q. Right. They have doctors in New Zealand, right?

A. I assume.

Q. Assume some of them -- do we need to look to see if there are medical doctors on Miles?

A. It's up to you, I'm in your hands. Whatever you would like.

Q. Why don't you look.

A. So it doesn't tell me on the authors who's a doctor and who isn't.

Q. But it usually has a little reference, and then you see their institutions they're associated with or M.D., Ph.D.

A. Yeah, it's -- well --

Q. Doctor, it doesn't -- I went down that track because I didn't think we were going to debate it.

A. Okay.

Q. If you can't find it --

A. I found it now, yes.

Q. Okay. All right. And there are doctors?

A. They're from the departments of medicine and then from obstetrics and gynecology and from psychiatry in -- actually they're in Australia, so we ought to correct that, they're not from New Zealand.

Q. Okay. All right. So if we go to page 1011 some of those -- the authors of the study, including people from the department of obstetrics, gynecology, and psychiatry actually conclude -- page 1011 -- that the alternative first line SSRI medications, Sertraline of Citalopram, should be considered as first line SSRI treatments in pregnancy and women of child-bearing age. Did I read that correctly?

A. You did.

Q. And in the Miles meta-analysis following their peer reviewed published methodology that's the conclusion they made, correct?

A. I assume they made that conclusion since it's in the paper.

Q. And you disagree with them?

A. No, I don't disagree with that necessarily.
Q. All right. Let's move to McDonagh.
A. I'd be happy to explain why, but -- that particular sentence is not something that intersects with my report that much.
Q. Okay. Let's move to McDonagh. July 2014 the agency for health care research and qualify, that's a branch of the Department of Health and Human Services, right?
A. That is correct.
Q. And this is a meta-analysis that examined, among other things, the risk of cardiac malformations associated with Zoloft use during pregnancy?
A. It did, briefly, yes.
Q. All right. And if we go to table 6, Doctor, and I think we've seen this before. Table 6, the meta-analysis found -- actually page 45, I'm sorry. A quote from page 45. Found that they pooled analysis --
A. Sorry, can I just --
Q. Yeah.
A. -- interpret you for a second?
Q. Sure.
A. You said page 45, but there is no table on page 45, so if you --

Q. Right. We're going to come back to table 6.
A. Oh, I'm sorry.
Q. I apologize.
A. You've moved around here, okay.
Q. I absolutely did.
A. Great.
Q. Page 45, Sertraline.
A. Yes.
Q. With me? This meta-analysis first found that pooled analysis of the seven studies that reported adjusted odds ratios resulted in no increased risk of cardiac malformations (table 6) but with statistical heterogeneity. Did I read that correctly?
A. You read that correctly.
Q. And so McDonagh actually did a further analysis to try to account for and look into this heterogeneity, right?
A. She tried to -- or she or he tried to remove it by doing a sensitivity analysis by looking at fewer studies.
Q. Right.
A. Which will of course inevitably reduce heterogeneity systematically as you peel them off.
Q. So they got that right. They're looking to reduce heterogeneity and they followed what you said

is a way to reduce heterogeneity.

A. Not really. It depends very much on how you select your approach to reducing heterogeneity.

Q. Okay.

A. My report says the right way to look at the statistical heterogeneity is try and determine the factors that explain the heterogeneity, because then you will have some knowledge about what the characteristics are of women in studies who show an increased risk and what the different characteristics might be in studies which show no risk, and that's not what they're doing.

Q. Well let's --

A. So this is not exactly what I would do, no.

Q. Not exactly what you'd do, but it's what they did?

A. It is what they did apparently, yes.

Q. And they published it and they subjected it to peer review, correct?

A. Yes, they --

Q. All right.

A. -- some -- as I said this -- early this morning, I'm not sure of the level of peer review on this publication.

Q. Okay. Let's look at the next sentence where

we talk about this sensitivity analysis, okay, Doctor?

Sensitivity analysis, first removing two studies that did not adjust for at least three of the four potential confounding factors identified for this review, resulted in a pooled estimate suggesting a reduced risk of cardiac anomalies with Sertraline (pooled adjusted odds ratio .76, 95 percent confidence interval, .59 to .97), but further limiting to the four studies that also indicated efforts to identify serious cardiac malformations yielded a pooled estimate of .76, 95 percent confidence interval, .57 to 1.0 P value .51. Actually that should be .051, right, Doctor?

A. It's certainly wrong, but that sounds plausible that it's just clipping -- it's just not significant.

Q. Okay. So the McDonagh authors concluded no increased risk or suggested a reduced risk for cardiac anomalies with Zoloft, correct?

A. That is correct, that's what they claimed.

Q. And you disagree with them?

A. I do disagree. Not so much with the findings per se, I disagree with the methodology that they used and the data they applied to reach that conclusion in light of what I myself have done, yes.

Q. Okay. Now if we go to table 6 now, which is page 44, the title of this table is, best evidence on risk of cardiac malformations with selective Serotonin reuptake inhibitors compared with non-exposure. Did I read that correctly?

A. Correct.

Q. And their finding for Sertraline or Zoloft is 1.08, confidence interval is .70 to 1.65, correct?

A. Yes, that is correct, you read it correctly.

Q. And because of the heterogeneity they did the sensitivity analysis, correct?

A. They did a sensitivity analysis, correct.

Q. And that yields the result of an odd ratio of .76, confidence intervals .57 to 1.0, correct?

A. Correct.

Q. All right.

A. That's the same number I think that you just read in the paragraph a minute ago.

Q. And so the table corresponds with the statements that they made is accurate?

A. That is correct.

Q. Okay. There's another meta-analysis, right, Dr. Wang 2015?

A. Yes.

Q. This one God smacked you?

A. It did.
Q. All right. Do we need to talk about Wang?
A. Well you -- I'm in your hands.
Q. Okay.
A. I'm happy to talk about it if you want.
Q. Let's briefly talk about Wang. Three studies, right?
A. Three studies, correct.
Q. Peer reviewed and published?
A. Correct.
Q. And you disagree with it?
A. Again, it's not so much the results, it's the fact that there are only three studies included in the meta-analysis with no real explanation of why all the other studies, including some of the major ones we've discussed at length, were excluded.
Q. Okay. And you disagree with -- it adds nothing to you?
A. Well of course a meta-analysis I can do it of those three studies myself, so from that point of view it doesn't add anything new -- they don't provide any new statistical insights into the data about those three studies that I was not aware of before. So from that perspective, yes, it doesn't provide a lot, and it's so incomplete.

Q. Incomplete because there's a bunch of studies and they only did three, right?

A. And the particular choice of those three too in terms of where they sit in terms of updates and overlaps, yes.

Q. All right. Let's move to your report in the Prozac litigation, Doctor, because there you did focus your review on numerous meta-analyses that reviewed and analyzed data relating to maternal exposure to Prozac during pregnancy, right?

A. Well as I just discussed before the break I focused my analysis initially -- or my analysis began with in a sense the meta-analysis that was provided by Eli Lilly themselves in their own documents. And there are others, as I indicated earlier, that I also looked at, including Miles, for example, and I think even McDonagh was -- commented about Prozac also. So those were also discussed in the report.

Q. Doctor, do you agree or disagree with the following statement. You focused your review on numerous meta-analyses that reviewed and analyzed data related to maternal exposure to Prozac during pregnancy?

A. I put -- I just answered that question, I believe. I focused my analysis initially on the Eli

Lilly meta-analysis, which is more complete than Miles, and then of course I included data from studies that were newer that were not incorporated in that. So, I focused my analysis on the entire body of evidence regarding the association between Prozac and cardiac birth defects.

Q. Tab 19, please. Doctor, this is page 5 of your Prozac report. Can we pull it out so everybody can read it, please.

A. Uh-huh.

Q. Let me know if I'm reading this correctly.

I focused my review on numerous meta-analyses that reviewed and analyzed data related to maternal exposure to Prozac during pregnancy. Did I read that correctly, sir?

A. You read that correctly.

Q. All right. And your review of meta-analyses included Miles and McDonagh?

A. Yes, as I just said, yeah.

Q. Okay. And let's look at your Prozac report on your findings from the Miles investigators. It's page 20 of your Prozac report. Okay. All right.

You say, existing -- these are the findings of Miles -- or at least this is based on the findings of Miles, right?

The existing research appears to implicate Fluoxetine and Paroxetine. This suggested that neither Paroxetine nor Fluoxetine should be used electively as first line antidepressant therapy, and those wishing to become pregnant or in the first trimester of pregnancy.

Did I read that correctly?

A. Yes, this is a quote from Miles, if I understand it correctly.

Q. Quote from Miles.

A. In my report, yes.

Q. Right.

A. Okay.

Q. And then you've got a dot, dot, dot, right?

A. Correct.

Q. And Mr. Zonies told us yesterday that the dot, dot, dot is very important, so let's look at what's --

A. Sure.

Q. -- dot, dot, dot. Let's go to Miles. And the dot, dot, dot actually says, "When Sertraline or Citalopram might equally be prescribed." Right?

A. It does, yes.

Q. Okay.

A. I don't see the point there. It's -- this

is a report about Prozac. I think the sentence is perfectly clear, but be that as it may.

Q. Okay. You in fact comment that that's quite a strong statement. It's significant enough for those authors to make that statement. In order words saying don't use these as first line, use these, right? You said that's a strong statement.

A. That's the statement the authors made, yes.

Q. All right. Now we heard this briefly so I'm going to try and just sum it up, Doctor, but instead of focusing on meta-analysis in your Zoloft report like you do in your Prozac report, one of the reasons that you don't focus on Miles in Zoloft is the methodological flaws, correct?

A. Correct. Correct.

Q. And you say in your report you don't find Miles scientifically reliable, right?

A. In terms of the results that you've spent some time reading a minute ago I think they're misleading to the Court and to people listening, because they're not reliable in the context of the whole body of evidence.

Q. All right. So actually if they're misleading in this court and you think they've gotten them wrong they're out in the peer reviewed published

literature, so anybody who picks it up is going to be misled by a peer reviewed published meta-analysis done by Miles. That's your opinion?

A. I think if they're interested specifically in the question of Zoloft and cardiac defects there's more room for misinterpretation because of the heterogeneity that we discussed yesterday. There's less room for misinterpretation with regard to Prozac, because there's far less heterogeneity in the results that Miles presents for Prozac.

So again, it's a contextual answer. The whole paper is not entirely misleading from beginning to end, and as I said, anyone can do their own meta-analyses of the studies that Miles considered, should they wish.

Q. And, Doctor, in the Prozac litigation, in that report, you refer to methodological limitations of Miles, correct?

A. Yes. And as we discussed yesterday, there was this confusion about the inclusion/exclusion criteria that Miles used that still remains uncorrected, as far as I'm aware, and the issue of heterogeneity.

Q. Sir, there's an affidavit from Dr. Large, one of the coauthors of the Miles study, saying they

used the appropriate inclusion/exclusion criteria and you got it wrong, right? You've seen that affidavit?

A. I did. And as I pointed out at the deposition when that was presented to me, that his statements -- and I think we discussed this yesterday -- his statements and the statements in the paper are contradictory. He has now apparently, I didn't know this, but from emails between your counsel, and he has agreed that it was written badly. We should look at the emails to use his language, but he has written it badly and maybe he should send a correction. I think that's the last I've heard of the story, but I don't know if a correction has appeared or not.

Q. So it's wrong in the peer-reviewed published and he got it wrong again when he said you were wrong?

A. In the affidavit, because as we discussed yesterday the paper specifically says the exclusion referred to excluding studies where some of the women in the control group were exposed to other antidepressants, in the affidavit he claimed that the inclusion/exclusion criteria used/excluded only studies where all of the women in the control group were not exposed to antidepressants. So it doesn't -- and as I've said many times, it doesn't really -- you know, it's essential, I'd just like him to tell me

what the actual inclusion/exclusion criteria area. To some extent, with all the new studies that have appeared Miles it's somewhat moot, because one wouldn't do a meta-analysis today, even if that were appropriate, on the studies that Miles used.

Q. Doctor, let's go back to McDonagh. Let's go to page 22 of your Prozac report, if we can, and how you describe McDonagh.

(Pause)

Q. All right. Again, this is your Prozac report referring to McDonagh. This is a report issued in July, 2014 and its stated objectives were "to conduct a systematic review to evaluate the benefits and harms of various pharmacological treatment options for depression during pregnancy and the post-partum period compared with each other with non-pharmacological treatments and with usual care or no treatment. I focused my evaluation and review on the Prozac-specific findings related to cardiac malformations and somewhat to major malformations overall. The sources of data review and study selection process were done through literature searches and review of abstracts and publications. Case reports, case series and single-group studies were excluded from the evaluation."

Did I read that correctly?

A. You read that correctly.

Q. Now, that's not how you describe McDonagh in your Zoloft report, correct? Let's look at that.

A. Actually, I don't think McDonagh was in my original report at all, but --

Q. That's fair. We discussed it and it came back --

A. Yes.

Q. -- and came in later.

A. Yes, because people wanted me to say something about McDonagh.

Q. Okay. Well, let's look at what you say on McDonagh and in your Zoloft report, in your updated report. "An additional meta-analysis was also carried out by McDonagh 2014 for the Agency for Healthcare Research and Quality. This is another meta-analysis suffering from methodological problems regarding how studies were included and excluded. Due to the study's brief section on Sertraline and cardiac birth defects consisting of only three sentences, it is impossible to fully assess the author's methodology."

Did I read that correctly?

A. That is correct.

Q. All right. Well, let's go and look at the

section on -- part of the reason you reject it on Zoloft is there's only three sentences. What on earth can we conclude from three sentences, right?

A. No, I just am trying to point out there -- and I'm not a big fan of McDonagh, I don't think that's a surprise to anyone in this room --

Q. It's no surprise to me.

A. -- whether I'm talking about Prozac or talking about Zoloft -- what I'm pointing out there, it's a very brief part of a much larger report.

Q. Right.

A. And to be fair to the authors, they were trying to study many, many questions, and so they were not able to describe their methodology in detail in the way you would expect in a paper like Miles, for example, or Wang for that matter, and they only have three sentences to do it. If you go into the body of the report, you can -- in the Prozac I said this is how they came up, as far as I understand it, with their studies, seven in the case of Prozac, that's all I'm saying.

Q. So it was brief, it was three sentences, not enough for you to evaluate, right?

A. Well, I think it's -- when you're reviewing a meta-analysis, as we've just spent some time talking

about with Miles, you would like to understand the inclusion/exclusion.

Now, as it happened with Zoloft, I was sufficiently familiar with all of the studies that could have gone into a meta-analysis to recognize in the references and their footnotes the seven studies they were using, but they don't describe why these seven, they don't tell me in the reduction that you spent some time going down when they did a sensitivity analysis, they're not explicit about how they -- which studies they removed. And so that actually made it hard to reproduce on my own any meta-analysis that could reproduce McDonagh as a result, because it's just -- they don't have enough space and they haven't described it. That usually wouldn't be satisfactory if you had a paper about Zoloft and cardiac birth defects.

Q. I understand. So not enough information on Zoloft, but you did have enough information on Prozac to --

A. There's the same --

Q. -- at least assess, right?

A. There's the same information in both, it's got the same level of quality. The fundamental difference in both Miles and in McDonagh comparing

Zoloft and Prozac is the heterogeneity of the information. The heterogeneity of the information is clearly statistically significant in Miles, it's not in Miles for Prozac. That's the difference, the fundamental difference. But with regard to the quality of the meta-analysis per se, it's the same for both. I have never tried to claim anything other than that.

Q. Are we talking about McDonagh or Miles?

A. We were talking about Miles. If you want to say McDonagh, there's the same issue occurs in McDonagh too.

Q. Okay, Doctor, I think this is referring to McDonagh when you talk about the three sentences.

A. Yes. Now, if you turn to table 6 on page 44, if you could put that up on the screen for us?

Q. Already been there.

A. Could you put it up on the screen so I can --

Q Sure, absolutely. The table 6 that we already discussed that has the two results, one before the sensitivity --

A. Table 6 on page 44. It was up a minute ago.

Q. Doctor, I promise you, I won't talk over you, if you won't talk over me.

A. That's fine. I'm just asking for table 6 on page 44, it's --

Q. Right. And table 6 is the "Best evidence" table, right, that one?

A. It's the one you just put up to read and comment on.

Q. Let's put it up again.

MS. YATES: If they're relying on me to find something, Your Honor, we're in trouble. It is --

THE WITNESS: Well, I can read from it, if you want. I have it right in front of me.

MS. YATES: No, let's put it up, so the Court can see it as well.

THE COURT: Well, I'm looking at a hard copy too.

MS. YATES: Are you? Okay.

THE WITNESS: Okay, great. So --

THE COURT: My eyes are not adjusting to the filmy program, it's very hard to read this.

MS. YATES: It's hard to read on -- yeah.

THE COURT: It's much harder than yesterday and I don't know if it's just a programming issue with working through the court system or not,

but it's hard. So I've resorted to paper, just like our witness.

MS. YATES: And I'm struggling a little bit, Your Honor, as you can tell when I look at the screen. So I'm tending to multitask here. Okay.

THE WITNESS: There it is.

BY MS. YATES:

Q. So table 6 that we already discussed, right, Doctor?

A. Yes. Now --

Q. And this is --

A. Wait a minute, I was --

Q. I'm sorry, I get to ask questions.

A. I think I was making the point, though. I wasn't waiting for a question, I wanted to bring this back up --

Q. Oh, I'm sorry.

A. -- in reference to my answer, and my answer was, the fundamental difference in Miles was the heterogeneity and you said -- interrupted and then said, but that's Miles, we're talking about McDonagh. So here's the table, it gives us information about heterogeneity from McDonagh. And you can see in the right-hand column, the heterogeneity, I won't bore you with what the i-squared statistic is, but it's -- the

larger it is, the more heterogeneity there is.

For Sertraline, you can 68 percent in that column, meaning the results that led to that meta-analytic odds ratio vary substantially, there's some much lower than 1.08 and there's some much higher. And you can see from Prozac or Fluoxetine, the heterogeneity is zero percent, it's actually also zero percent for Paroxetine and Paxil, meaning there's very little heterogeneity. That's fundamentally the reason why you might treat the data differently for Zoloft than you might for Prozac or, for that matter, for Paxil.

Q. And, Doctor, we went through this, but just to be clear, the reason there is a sensitivity analysis under Sertraline is because of the finding of heterogeneity, correct?

A. That's one reason they did it, it's not the reason they -- the sole reason they did it.

Q. Okay, one of the reasons.

A. Correct.

Q. And when they did the sensitivity analysis, the heterogeneity goes to zero percent, correct, Doctor?

A. Well, do you really think that's a plausible way to deal with heterogeneity? The issue -- how they

dealt with heterogeneity here is they simply took the low values of the odds ratio, the ones that were most alike, of course the heterogeneity goes away. A grade school student could do that, just put the red blocks together. That's not a statistically sophisticated or appropriate way to deal with heterogeneity. Let's just find a way to get the results in the meta-analysis to a point where they all look alike and throw the other ones out, that is not to me an appropriate methodology. Anyone could do that. As I said, as you remove studies, systematically that 68 percent there, as you go from seven to six, will go down. Whatever one you pick, if you take two out, it will go down some more. It will go down a lot if you hand pick -- I'm not going to say cherry pick, but if you hand pick the studies, in this case I think it was four of the seven, they picked -- or they ended up with the four that were the most similar, so the heterogeneity is gone. That's why they get this kind of strange result that Zoloft is protective for cardiac birth defects. There's not a single other paper that I have read that suggests anywhere that Zoloft reduces the risk of a cardiac birth defect by 24 percent.

So it's just not a plausible

methodology in this meta-analysis to hand pick four studies that look the same, that all have low values, and get rid of the heterogeneity. That's actually what I was trying to get at yesterday where averaging can really obscure the truth. It's just not appropriate methodology.

Q. Sir, I'm not a mathematician, I couldn't do this, and if I look at sensitivity analysis that is in the table you wanted me to bring up, I see a zero percent heterogeneity after the sensitivity analysis. Did I read that correctly?

A. As I indicated, you read that correctly. And I think you understand now why I feel so strongly that that's an inappropriate way to deal with heterogeneity.

Q. Have you written to the journal saying this is wrong, this is ridiculous, a grade school student could do it?

A. I'm working my way through the places that Pfizer suggests I write to. It would be much more powerful, in my opinion, if Pfizer themselves, now that you understand why this is misleading, if Pfizer themselves would take on this, it would have much more weight than I. I've already -- I'm working my through it. I've contacted the FDA, I'm contacting

Huybrechts. I will get to this if you wish me to, but I'm -- you know, I have 24 hours a day.

Q. You've contacted the FDA?

A. I have asked for my report to be sent to the FDA, yes, because Pfizer urged -- asked me that same question at trial. You feel strongly about this, you have an opinion about causation, have you told the FDA? I answered truthfully that I had not at that point. As soon as the trial was over, I asked counsel if they would be willing to release my report to the FDA, which I believe they did.

Q. Do you know if counsel has released your report to the FDA, sir?

A. You would have to ask counsel to confirm that, not me, because I didn't physically put it in an envelope, but I asked them to do so. Now, they told me they did, but you'd have to confirm with them.

Q. Do you have a communication from counsel indicating that they have sent it to the FDA?

A. You'd have to ask counsel the communications.

Q. No, I'm asking --

A. They've told me verbally.

Q. I'm asking you if you have written communication from counsel confirming that they've

submitted your report to the FDA?

A. They have told me verbally on multiple times when I have asked.

Q. So you don't have anything written?

A. I don't have anything written, they may well have something written.

Q. All right, let's go back to where we were before we went back to table 6. So we were back discussing the fact that you're clearly critical of the methodology in McDonagh and part of your criticism was also that there's only three sentences on it, right --

A. But I'm not a big --

Q. -- we were there?

A. -- I'm not a big fan of the meta-analysis for either Prozac or for Zoloft, that is correct.

Q. All right. Well, let's take a look at McDonagh and the section on Prozac, because you did review and comment on it in your report on Prozac as part of your review. So if we go to Fluoxetine, Prozac, that's the entire section, Doctor, on Fluoxetine, correct?

A. Is this a quote or from my report? I'm sorry, I lost you a little bit.

Q. I'm sorry, this is actually from McDonagh.

So if you want the hard copy, it's under M for McDonagh.

A. Your Honor, I have the paper, is that -- I can't read the page numbers.

THE COURT: Isn't that the same page as table 6?

MS. YATES: Your Honor, that's a very good question.

THE COURT: I think it is.

MS. YATES: 44 to 45, yes, it is.

BY MS. YATES:

Q. Doctor, you should be there.

A. I'm on 46 with the table, but --

THE COURT: Right below it.

MS. YATES: Right below it.

THE WITNESS: Okay.

BY MS. YATES:

Q. That is the entire section --

A. Oh, table 6. Okay, I got it. Thank you.

Q. That's the entire section in McDonagh on Prozac, correct?

A. Correct.

Q. All right. I counted five sentences.

A. On Prozac?

Q. Yes.

A. Yes.

Q. I actually counted 128 words. Are you with me?

A. I'm sure.

Q. Okay. Let's look at the Sertraline or Zoloft section from McDonagh. That's the entire section on Sertraline, right?

A. Correct.

Q. Three long sentences?

A. As I indicated, yes.

Q. All right.

A. I did that counting.

Q. 143 words, I did that counting.

A. I didn't do that one.

Q. All right.

A. Key distinction, heterogeneity. Just think heterogeneity every time you go back to Prozac and Zoloft.

THE COURT: I think we're going to wait for a question.

BY MS. YATES:

Q. I'm not thinking heterogeneity, Doctor, I'm thinking what happens when they do a sensitivity analysis because of heterogeneity, right? They recognized the issue and they did something to try and

correct for it, that's what's in my mind.

A. Yes, but you have to do it appropriately.

Q. They did it wrong?

A. You have to use the appropriate methodology.

Q. Understood. You think they did it wrong?

A. I think it's misleading the way they did it, yes.

Q. Now, if I'm just -- if I applied your methodology and I looked at Miles and McDonagh, you know, if I focused on meta-analyses, as you did in Prozac, but now I'm going to do it in Zoloft, you would not be able to conclude that Zoloft increases cardiac -- the risk of cardiac defects, correct, if we just looked at the meta-analyses?

A. At the individual studies in the meta-analysis or just the summary results?

Q. The meta-analyses.

A. The summary results.

Q. The meta-analyses.

A. Well, the meta-analyses involve individual studies. Are you saying if I just focused on the summary results in --

Q. The results that refer to the studies in the meta-analyses, correct.

A. If you -- let me put it in my own words. If

you relied solely on the summary results, the meta-analytic averages that Miles and McDonagh report, you certainly would not conclude that Zoloft causes cardiac birth defects. If you looked deeper at the individual studies, you might come to a somewhat less definitive opinion. And when you looked at all the data, including the studies that are not included in Miles and McDonagh, which there are several major studies now, you would come I think to my opinion, at least I would come to my opinion.

Q. But you agree, Doctor, that the studies on Zoloft are equivocal, right? You've testified to that.

A. Well, there's no question, it's not every study coming in with the risk doubling and clear, I suspect we wouldn't be here if it was unequivocal.

Q. Right.

A. You must believe it's equivocal or you wouldn't be spending your time here. So of course the evidence is equivocal, that's why you need a statistician to assess and make inference from data which has uncertainty attached to it. That's what I'm trained to do and that's what I've tried to do in this case using appropriate methodology.

Q. Doctor, you testified with regard to

Avandia, correct, you sat in the witness chair?

A. Well, I couldn't remember exactly, as I said yesterday, but I did testify in a hearing about Avandia, yes.

Q. And in the Avandia litigation you also looked at meta-analyses, correct?

A. I did. And in that case there was a major meta-analysis -- now, this is -- my memory is now -- this is going back quite a ways -- there was a meta-analysis, if I recall, by GSK, the manufacturer of Avandia, on -- they had several randomized clinical trials and they had done at various points meta-analyses as they got more trials in. And then there were some published meta-analyses in the literature by authors outside of GSK that were looking at similar questions, the Nissan (ph) meta-analysis and the Seng and Ferburg (ph) meta-analysis of Avandia and the risk of heart attacks and stroke.

Q. And in the Avandia hearing you told the court that "meta-analyses are useful because they are an appropriate way to combine information to see if there's a persistent pattern that adds up to something of concern that reaches statistical significance," correct?

A. Yes. And in the context of randomized

clinical trials, that's certainly a true statement. As I testified yesterday, the value of meta-analysis in randomized clinical trials is that in a sense all studies are on an equal footing, at least with regard to compounding, because randomization removes the possibility of compounding, at least to some considerable extent because of the randomization. That's one thing.

The other issue in the Avandia case that was clear is these were all small trials. None of the Avandia trials that I testified about were designed to look at the issue of does Avandia increase the risk of heart attacks. This is not similar to the current case where most of the papers we've been discussing have been targeted specifically, in fact you read out the objectives of some of them, that they're specifically looking at the safety of SSRIs and birth defects. The trials in the Avandia meta-analysis were not designed to do that. They were small efficacy trials to measure the effect of Avandia in treating diabetic patients, so you get very few heart attacks. And I went through this at great length in that litigation. That's where meta-analysis now starts to play a quite different role than it does here.

So there are clear distinctions between the use of meta-analysis in the Avandia and the use of meta-analysis here. In both cases they should be done appropriately, of course, and any methodology can be misappropriated.

Q. Doctor, do you remember my question?

A. I do. You asked me about my testimony and using -- did I use meta-analyses in my work on Avandia, and I said yes and here's what I did and why I used meta-analyses in that litigation.

Q. Let me ask my question again, because that wasn't my question. Didn't you tell the court in Avandia that "meta-analyses are useful because they are an appropriate way to combine information to see if there is a persistent pattern that adds up to something of concern that reaches statistical significance"?

A. Yes, and that's as I -- I did hear your question correctly and that's what I answered. In the context of that report where you're reading from, that's a context of randomized clinical trials, all small, with regards to detection of heart attacks. If you -- I don't know if the Judge's memory is any better than mine or yours, but in the Avandia litigation most of the clinical trials or many of them

had zero heart attacks. That would be equivalent in this litigation of looking at a study --

Q. Doctor --

A. -- of Zoloft and cardiac birth defects in which there were no cardiac birth defects observed. So it's a quite different context. In the context of randomized clinical trials, each of which have very little information on the outcome, very few heart attacks in the Avandia case, you're almost obligated to turn to something like a meta-analysis. All I'm saying in addressing your question is that's the context where that statement it's useful to use meta-analysis to combine studies, many of which have zero outcomes, into seeing whether there's something signal. That was the approach done by GSK, by Nissan and by Seng and Ferburg. That's a different context from where we are today in this particular litigation.

Q. So in Avandia you relied on and analyzed meta-analyses, in Prozac you relied on and analyzed meta-analyses, and in Zoloft you looked at them and you said no, correct?

A. No, that's I would say a mischaracterization of my methodology. I looked at the meta-analysis in the Zoloft litigation, they're covered in my report.

Q. And you've said in your testimony you've

rejected them?

A. If you could just let me finish and then -- that would be okay?

Q. Absolutely.

A. So you said I did something differently in the three settings, Avandia, Prozac and Zoloft. In all three of them, there were meta-analyses done by other individuals. In Avandia, I actually did my own meta-analysis in addition. In all three of them I took accounting of their methodology, their findings, their insights. And in sum, as I discussed at the end of my testimony yesterday, you ought to be situational to the extent you can tell the different between context, you ought to be able to tell the difference between in Avandia you're dealing with randomized clinical trials and in Zoloft you're dealing with observational studies.

You shouldn't treat meta-analyses and interpret them as a statistician exactly the same way in both those contexts, any more than, as you pointed out earlier this morning, you shouldn't treat an observational study the same way as you would treat a randomized clinical trial. You're going to use different statistics. It doesn't mean I ignored the meta-analyses in any one of these litigations or in

any of my other professional work, it's just you've got to interpret them and take account of their value and quality in the context.

Q. Doctor, there were also observational studies in Avandia that you looked at?

A. Well, we're going back about ten years. My memory is I didn't look at the observational studies in Avandia. But I'm happy to be corrected, but that was my memory.

Q. Let's go to -- let me just show you some testimony and see if it refreshes your recollection, in Avandia.

A. Sure.

Q. Let me see if I can do this.

MS. YATES: Your Honor, may I approach?

THE COURT: You may.

BY MS. YATES:

Q. It's tiny print, I apologize, but this was your Avandia testimony before Judge Rufe, In re Avandia. And so you're talking about, "We are fortunate because there are randomized controlled trials," right? We talked about that. And then subsequently, "then I would go on and look for information about the observational studies." Does that refresh your recollection that there are a number

of observational studies?

A. Oh, there certainly were, I have no -- there are certainly a number of observational studies about Avandia, but the body of my report and my testimony before Judge Rufe was about the randomized clinical trials.

Q. Oh, but you did review them, right?

A. I did review them, but I didn't put them in my report. I focused my report, to use your words, on the randomized clinical trial information, for which there was a lot, there were a lot of random -- there were close to 50, if my memory is correct, of randomized clinical trials. That was the focus of my report and that's my memory. I didn't spend any of my report discussing the observational study information, they're clearly is some.

Q. Right. And so -- okay, I'm not going to belabor it.

All right, let's go back to see if we can agree. You advised the Court in Avandia that "there are formal techniques in a meta-analysis that are designed to make sure studies are weighted properly." You agree with that, right?

A. Yes, there's -- meta-analysis is an averaging processing, as I indicated, and it's going

to weight different studies --

Q. Right.

A. -- differently because of the -- you know, for example, sample sizes can be substantially different.

Q. Because the little guys don't have the same weight as the big studies?

A. That's a nice way of putting it, yes.

Q. Okay. "And these techniques make sure that you don't make the improper mistakes of averaging results, so that no study has an undue influence," correct?

A. It should have its influence based on the weighting scheme, which is usually a sample-size driven scheme, but not always, sometimes it's a little bit more sophisticated.

Q. And you've testified in this case that you can't do a meta-analysis because of this heterogeneity, correct?

A. Well, I'm not saying you can't do it, you can, it's just you have to be very careful in interpreting it because the averaging that is involved, weighting or not, can mislead you when you rely on the results of the summary when there's substantial variation in the individual trials.

Q. I just want to be accurate here.

(Pause)

Q. All right. Do you agree, Doctor, that based on the heterogeneity the problem that you have in Zoloft is that the averaging that meta-analyses does pretty much gets you nowhere, that's your opinion?

A. No, that's -- maybe -- that's not my words. I wouldn't say gets you nowhere, it's just you have to pay attention to the heterogeneity in interpreting the results that it gives. As I tried to make this clear yesterday, if you have two studies, one of which shows an odds ratio of two and one of which shows an odds ratio of 0.5, let's say equally weighted to make it simple, and you do a meta-analysis and you come out and report in the literature an odds ratio of 1 and interpret no risk, first of all, that's incorrect, an incorrect statistical interpretation, and it's clearly misleading because half of your women in the study had an odds ratio of 2. No one had an odds ratio of 1, as it happened. So that's why it's misleading. And, I mean, I can go on in greater detail as to why it's so misleading, but I thought that made it clear that in those kind of situations you can't resort to meta-analysis to resolve the inconsistency or the heterogeneity of the two studies.

Q. So let's take a look at your deposition. Do you remember having your deposition taken in a Zoloft case called Trace Foster? It was pending in St. Louis.

A. I don't recall, again, the details of the specific depositions.

MS. YATES: Your Honor, would you also like a copy of the transcript?

THE COURT: If you have it, yes.

(Pause)

THE WITNESS: Thank you.

MS. YATES: And we can put it up on the screen.

BY MS. YATES:

Q. And if you turn to page 103, Doctor, starting at line 7. Question, "You're perfectly capable of searching PubMed and a priori to find set of inclusion/exclusion criteria and accumulating the data the same way Miles and the same way McDonagh did, correct?"

Answer -- and the answer goes on for a bit, so bear with me -- "Well, but you're misinterpreting my answer. That certainly was not the obstacle. The obstacle is the data itself does not lend itself for a meta-analysis to be useful. The

meta-analysis is an averaging process. If you want to take an apple and an orange and average it, there's no obstacle to doing it, you can do it. You can take orange juice and apple juice and mix them together, there's no physical obstacle to doing it. Does it make sense? Sometimes averaging does. I've lived most of my life where averaging is terribly valuable, but the statisticians that have known for a long time that averaging can be horribly misleading. And in this case, with this amount of heterogeneity across studies, averaging gets you pretty much nowhere. So this is not a prime candidate for doing an effective meta-analysis, in my view."

Did I read that correctly?

A. You read that correctly and that's exactly what I said yesterday.

Q. Doctor, so you said there, when you've got this heterogeneity problem, it's like mixing apples and oranges, right?

A. Yeah, that would be like the 0.5 and the 2 in my hypothetical example.

Q. Right. Do you recall that in Avandia you were asked about heterogeneity and whether it was like mixing apples and oranges?

A. I can't recall the details of the discussion

ten years ago.

Q. Isn't it true, sir, that you told the Court that it's not like mixing apples and oranges, but rather mixing different types of apples?

A. Well, I'd have to see the testimony.

Q. Okay.

A. It does sound like something I would say. And that would refer to -- the idea of apple and an orange is heterogeneity, right? An apple is quite different. If I held them in my hand, you could tell the difference, right?

Q. I sure hope so.

A. If I held two different varieties of an apple in my hand, could you tell the difference?

Q. Possibly.

A. But maybe not, right?

Q. I could tell the difference in those wine glasses.

A. Yeah, but that's an apple and orange. Let's not change the metaphor. If I had two apples, distinct varieties of apples, you probably couldn't -- well, maybe they look enough the same, maybe I can combine these. That's exactly what I'm saying in this testimony here, that's exactly what I said yesterday, that's exactly what I'm saying now. When you're doing

a meta-analysis averaging, it's fine in all other things being equal to do it when you have no heterogeneity, because then the averaging is valuable, you're not mixing a 0.5 and a 2 and coming out with this distorted in-between value that no one experiences. And the value of meta-analysis, as in Avandia, is you get the increased precision that you get from combining multiple small studies.

So it's not that meta-analysis in itself is supposed to give you a magical different answer from the studies, that's not the purpose of meta-analysis. The purposes of meta-analysis, if done correctly, is to take homogeneous phenomena, each of which is imprecise, average them, and then you get a measure of the phenomena you're interested in, an odds ratio, but with much more precision. That's the point of averaging always, that's the point of meta-analysis, but you don't do it and mislead people when there's so much heterogeneity. That's what I said in this you just read me, that's what I said back in the Avandia case, that's what I said yesterday, and that's what I'm saying today.

Q. All right, Doctor, let's go to, I believe it's the same transcript, page 31.

MS. YATES: Is it the same transcript?

UNIDENTIFIED SPEAKER: No, that's (indiscernible).

MS. YATES: Oh, I'm sorry. It's not the same transcript, so I need another transcript.

BY MS. YATES:

Q. Doctor, we're now going to the Avandia transcript.

A. Okay.

Q. If you would turn to page 31, line 6. Question, "The other thing I wanted to ask you, is it like" --

A. I'm sorry, could you -- which page was it?

Q. I am so sorry. Page 31 --

A. 31, thank you.

Q. -- line 6.

A. Thank you.

Q. And actually we can -- you'll see on the middle of page 30, "Yesterday the word heterogeneity came up, right? So let's just give a little bit of context there."

Now we can go to page 31, line 6. Question, "The other thing I wanted to ask you about, is it like mixing apples and oranges?"

Answer, "Well, of course the key thing in a well-conducted meta-analysis, one of the

limitations I think I refer to here is that the clinical trials that you are combining or observational studies, if it's a meta-analysis of observational studies, are not identical, they don't in fact one -- you can view that as a strength and a weakness. They are not identical population, they are not sampling from exactly the same population. The eligibility criteria for the trial that was designed for an efficacy reason may vary from trial to trial somewhat, they are done in different places.

"As I say, this is a weakness because you are now trying to mix things that were collected in different places. It's also a strength because, as we heard yesterday, one of the important issues in causation is seeing is a phenomena, is there any idea of a risk replicated in different populations, because that is going to strengthen your belief that this is something causal and not peculiar to a particular trial or a particular population.

"So one of the limitations, as I said, and strength is you are mixing these things. It's not mixing apples and oranges, however, if I can use that analogy, it's mixing different varieties of apples. All of these studies have the same drugs applied to the treatment arm, they were all by and large, with

some notable exceptions, studying diabetics, they were all essentially, when the data was pulled out on adverse events, they were -- all these investigators were honestly, I think, trying to get at the same question. So this was not really trying to pull things from out of a hat and sort of jam them together, this was -- most of these meta-analyses, not all of them, but most of them were well conducted, thoughtfully, and trying to answer the question and summarize the information."

Did I read that correctly?

A. I think you did.

Q. Thank you.

(Pause)

Q. Now, Doctor, I think we're well aware of your criticisms of the meta-analyses on Zoloft, but you did a mini-meta-analysis, right?

A. I did, as I described yesterday, in the "paused" analysis we had two major studies that allowed you to independently look at the question of comparing women on Zoloft and comparing those who continued to use Zoloft during the first trimester by some definition versus those who didn't, and I combined those two in front of the Court yesterday.

Q. Right. So there's a couple of steps here,

let's see if we can go one at a time. You performed a calculation or a reanalysis of some of the Huybrechts data comparing, what you say, women who filled the prescription in the first trimester and women who did not fill a prescription in the first trimester, right?

A. One or more prescriptions filled, yes.

Q. And this analysis or calculation is not part of the peer-reviewed published study of Huybrechts, right?

A. Well, the data are there in the peer-reviewed publication, that particular calculation is not.

Q. Right, that was my question. And it's not part of the investigator's methods, correct?

A. I don't know if it's -- the investigator certainly deliberately tried to separate out these women that had at least one prescription filled during pregnancy, because I believe in their sensitivity analysis they believed that was a more rock-hard measure of exposure if you actually filled a prescription. You not only were exposed in that you had a previous prescription that took you through the first days after conception, but then you also filled one. From their sensitivity analysis perception, they thought that was a more definitive measure of exposure

and that's what they used it for. And I used the same data, but in a slightly different way.

Q. Sir, your calculation was not part of the investigator's methods set forth in the peer-reviewed published article?

A. As I just indicated, yeah, the data was there in the supplement, but not that particular calculation, that is new, yes.

Q. And in fact Dr. Huybrechts has referred to reanalysis as a post hoc subgroup analysis, correct?

A. As well as referencing it as interesting.

Q. And after the fact, post hoc -- I took a little bit of Latin -- means after the fact, right?

A. I actually took a little bit more Latin than you --

Q. There you go.

A. -- but I'm surprised you didn't.

Q. I rejected it. I looked at it and rejected it. You haven't published your reanalysis, sir?

A. No, I've asked -- as I indicated yesterday, I believe to take the data from someone else's paper without approaching that author directly and asking them to collaborate would be -- not be my scientific approach. So I have asked the author if she would be willing to publish them with me, because it's her data

and she knows that data, and I think that would be the right way. And as we discussed yesterday, we're en route somewhere, I don't know how it will play out in the end. She may not wish to be involved given how much contact she's had from lawyers in this case.

Q. She politely declined, right?

A. No, at the last email she actually indicated that she would maybe see if some of her team could help.

Q. Let me back up. When you asked her to be a coauthor, that email politely declined, correct?

A. Yes, she said she had too many other projects. If you want to look at the emails, please do. And then at the last email, when we had worked through what I was getting at, she said that's an interesting possibility or something, and then I'll see -- I'll bring it up to my team and see if someone else can. I assume she's too busy.

Q. That was your request for the data?

A. No, that was the request to publish the data -- well, that was my request for them to run the analysis --

Q. Right.

A. -- adjusting for compounding. I assumed if they did that they would be willing to stand behind

their work and co-publish, but I can't --

Q. That wasn't the question, was it --

A. -- I can't --

Q. -- Doctor?

A. If you could just let me finish. I couldn't -- I can't speak to that. We're in the middle of something here. I wrote to Dr. Huybrechts saying here's an interesting analysis, it's your data, would you coauthor? She said, I'm too busy, and anyway it doesn't adjust for compounding. I said, exactly, that's why I need your help and would you be -- I need the raw data. She said, I'm too busy, I'll see if my team can help. Now, whether that leads to a publication that they want to be associated with or not, that's for the future to decide.

Q. You have no idea right now, right?

A. Whether it will be done? Well, I can't do it and I have no control, I think is a better way of putting it, yeah.

Q. And the data you extracted was from the supplement of the Huybrechts study, right?

A. That's right, the online supplement.

Q. And you defined some users in that supplement as "paused"?

A. And I put paused in quotes because --

Q. So did I.

A. Yes, and so did you, because the word paused comes from Jimenez-Solem paper and --

Q. I'm coming to that, I promise.

A. I understand. I --

Q. I'm just trying to do this -- right now the questions are this long and the answers are really long, Doctor, and I really would appreciate it if you could focus a little bit more on my question. I will get there and then your counsel has a chance to do a redirect.

A. I'm sorry, I'm a teacher, I can't help it, I can't turn it off. That's why I put the word paused in quotes, it's a slightly different definition than what's used in Jimenez-Solem --

Q. Precisely.

A. -- where they use the word paused.

Q. So, number one, Dr. Huybrechts did not define this population as "paused," correct?

A. She didn't use that word, that is correct.

Q. And, number two, your definition of paused is different from the Jimenez-Solem definition, right?

A. Yes, as I just indicated, yes.

Q. And as you said, Dr. Huybrechts pointed out, you haven't adjusted for compounding, correct?

A. And we discussed that yesterday and the rest of the story.

Q. Doctor, yesterday there were a couple of slides, pie charts -- and I'm sorry, I only have black-and-white, but if I can use the Elmo, maybe that's easier to see. Okay, let's see if I can -- this pie chart was shown. This is your reanalysis of the Huybrechts data. And I apologize, that's my handwriting, "Jewell's definition of paused," we've already gone through that. And you have an odds ratio of 1.87, confidence level is 1.07 to 2.39, p value of 0.02, right, that's what you showed us yesterday?

A. Yes, I showed two of these, I believe, and this is the one, to be precise, that refers to the, quote, "paused group," I mean, the exposed as filling one or more prescriptions.

Q. Right. There was another one that talked about, after Dr. Gibbons commented, you went and did two or more, right?

A. Correct.

Q. But then we saw another slide, "Meta-analysis, Huybrechts and Jimenez-Solem." Huybrechts scored odds ratio 1.9, confidence level of 1.1 to 3.3.

A. Could you show me the previous slide, just so I can --

Q. Yeah.

A. -- because that's where I think you're going. Yeah, that doesn't look right.

Q. It doesn't look right, does it, Doctor?

A. Yeah, that's -- one of those is --

Q. Do we know which one is wrong?

A. Well, it will take a minute, because if I could take logs I could do the symmetry. Maybe Dr. Kimmel can do it for me, he's better at that with his eye. I can't tell with -- I think to be fair, I should correct one of those slides after I've had a chance to be in a dark room for two minutes.

Q. Okay, all right. One of them is wrong, we don't know which one?

A. Yes. The upper bound there looks incorrect on one of those.

Q. Okay. And just so we're clear, based on your communications with Dr. Huybrechts, you did not mean your unpublished reanalysis to supersede Dr. Huybrechts' big published study, right?

A. No, and I told her that of course, I didn't intend that.

Q. Right. When you did your meta-analysis, do you know if you used the correct numbers?

A. Which meta-analysis?

Q. So you --

A. Oh, you mean the two studies?

Q. Yeah.

A. I would have used the raw data itself, not the summary results. So I did it myself using the raw data, not -- so it's a transcription error in one of those upper bounds.

Q. All right.

MS. YATES: Your Honor, I am about to move on and I can hopefully tighten things up. I am happy to go on or I'm not sure --

THE COURT: Well, it is a lunch break time.

MS. YATES: Lunch break? Okay.

THE COURT: And I think we should take the hour again. If that's not enough, let me know, because we can easily come back at 2:00, but it is appropriate to break now for our lunch recess.

So why don't we get back here in an hour and assess where we are, and that would be ten minutes to 2:00.

MS. YATES: Thank you, Your Honor.

(Proceedings recessed at 12:49 p.m.)

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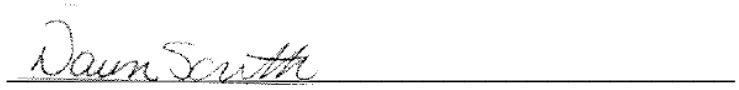
CERTIFICATIONS

I, Sheila G. Orms, certify that the foregoing is a correct transcript from the official electronic sound recording of the proceedings in the above-entitled matter.

Dated: September 1, 2015

Signature of Approved Transcriber



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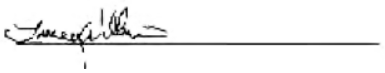

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